

In the Specification

Please amend the specification as follows:

On page 1, please amend the section titled RELATED APPLICATIONS as follows:

RELATED APPLICATIONS

This is a Continuation Under 1.53(b) of U.S. Application Serial No. 08/522,336, filed November 9, 1995, now U.S. Patent No. 6,287,863, which is a U.S. National Stage filing under 35 U.S.C. 371 of PCT/US94/02752, filed March 14, 1994 (published as WO 94/20608 on September 15, 1994), and which is a continuation-in-part of Application No. 08/194,208, filed on February 7, 1994, now abandoned, which is a continuation-in-part of application No. 08/130,638, filed on October 1, 1993, now abandoned, which is a continuation-in-part of application No. 08/097,721, filed on July 26, 1993, now abandoned, which is a continuation-in-part of application No. 08/060,568, filed on May 12, 1993, now abandoned, which is a continuation-in-part of application No. 08/030,766, filed on March 12, 1993, now abandoned, which applications are incorporated herein by reference.

Please amend the paragraph beginning at page 3, line 27 as follows:

Previously, the applicant filed patent applications (~~pending~~) covering the Method of Gene Transfer Using Retrotransposons (USA/07/603,635, filed Oct. 25, 1990, now U.S. Patent No. 5,354,674 and subsequent continuation application; also WO 92/07950), which described the first use of a nonviral mobile genetic element (VL30) for intercellular gene transfer and expression. Previous vectors had used replication-competent or defective viruses derived from a replication-competent oncogenic virus family, this facilitating recombination and oncogenesis. The vector of choice until now, Moloney murine leukemia virus (MoMLV) is also the vector most commonly used in helper cell lines, including those currently being used in human gene therapy (Miller et al., Mol. Cell. Biol. 6:2895 (1986); (USA 4,861,719). The instant invention.

describes new retrotransposon VL30 vectors which are made useful for human gene therapy through a number of modifications and improvements.

Please amend the paragraph beginning at page 13, line 27 as follows:

FIG. 4 illustrates a vector for producing a rearranged gene product in a recipient but not a donor cell;

FIGS. 4 and FIG. 5 are diagrammatic illustrations which depict a method for introducing a gene which produces a toxic or rearranged gene product in the recipient, but not the donor cell;

Please amend the paragraph beginning at page 14, line 2 as follows:

FIGS. 7 A-C illustrate stable integration of VLPPBN DNA after transfer into recipient cells. Panel A shows the unique 2 kb *Xho*I fragment that reacts with a *neo* probe (lane C is a control). Panel B shows digestions with *Bgl*II and Panel C shows digestions with *Stu*I.

FIG. 7 D shows the limited potential for methylation of CpG sequences in the NVL3 promoter compared to MoMLV and ALV;

FIGS. and 8 A-B are black-and-white photographs which show physical evidence that the vectors are efficiently and stably introduced and are abundantly expressed as RNA from the VL30 transcriptional promoter in the recipient cells. Panel A shows *neo* RNA expression in three VLPPBN transfected clones (lane 3-5) relative to a pSV2neo positive control (lane 1) and a negative control (lane 2). Panel B shows the blot in panel A rehybridized with a VL30 probe;

Please amend the paragraph beginning at page 43, line 26 as follows:

The disclosure above, and the explanation thereof were previously not known to vectorologists. For example, Mulligan *et al* disclosed a splicing retroviral vector which gave high titers and provided excellent protein expression (WO 92/07943; Guild *et al*, & USA/07/607,252). However, the reasons for high expression, although associated

circumstantially with a splice acceptor site, were not disclosed. In fact, the cryptic splice site was apparently included in the vector by accident. Similar vectors have since been constructed by other investigators. The present disclosure permits investigators to manipulate the vector to obtain the correct blend of expression and packaging by understanding the methodology described.